Remarks

Claims 12-35 are rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement in view of Taira, *No To Shinkei*, 44(1):61-63 (1992) (Abstract).

Applicant respectfully traverses the rejection and submits herewith the entire Japanese article of Taira, *No To Shinkei*, 44(1):61-63 (1992) and a full English translation of the Japanese article entitled Taira, *Brain and Nerve*, 44(1):61-63 (1992) in the Information Disclosure Statement filed concurrently herewith.[1]

Taira's Abstract (upon which the rejection is based) reports that two patients who were receiving zonisamide for the treatment of **epilepsy** experienced side effects of tremors. Taira's journal article reports that the

> development of tremor and involuntary movements were reported in its [zonisamide] package insert, *but the details have not yet been investigated.* The author experienced two cases of tremor *thought to be induced* by this new drug....

See Taira journal article at Introduction (Emphasis Added).[2] However, Taira reports only the experience of two particular patients. One of skill in the art would not consider Taira to teach or suggest, as is implied by the Examiner's reasoning, that the experience of these two individuals should be applied to all, or even to a substantial number of, patients generally. Taira is a study of two patients. Taira never reports how many patients had been treated for **epilepsy** with zonisamide.

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[1] To the best of Applicant's knowledge, information, and belief, the English language translation is an accurate translation of the Japanese article.

[2] The zonisamide package insert identifies tremors as a possible side effect and also states that zonisamide is indicated as an adjunctive therapy in the treatment of partial seizures in adults with **epilepsy**. *See* "Zonegran (zonisamide) Package Insert" submitted in the Information Disclosure Statement filed concurrently herewith.

Taira's journal article also reports that in the two patients he analyzed:

> [V]alproic acid was administered prior to the addition of Zonisamide. *We cannot deny the possibility that tremor appeared due to the synergistic effect of these two agents.* In fact, valproic acid alone is known to cause tremor...."

See Taira journal article at "Discussion," right hand column, first full paragraph (Emphasis Added).

Contrary to Taira's Abstract, Taira's full journal article casts doubts on whether zonisamide causes tremors because (1) the details of zonisamide causing tremors in **epileptic** patient had not been investigated and (2) the two **epileptic** patients in the study may have experienced tremors from the synergistic effects of valproic acid and zonisamide.

The pending claims are directed to the treatment of **tremors** in patients. The pending claims are not directed to the treatment of **epilepsy**, as described in Taira. Applicant respectfully directs the PTO's attention to Example 5 in the specification which provided human data showing the efficacy of zonisamide in treating **tremors**, i.e., as recited in the claims. Example 5 (specification at page 16, lines 5-18) states:

> Zonisamide was used in treatment of patients at an outpatient neurology clinic, which provided the following results. Adverse reactions experienced in treatment were GI upset, somnolence and skin rash. Kidney stones and anhydrosis (lack of sweating) were not encountered in the patients treated. For intractable essential tremor, 10 patients (age range: 46 to 82) were identified who were either intolerant to, or failed on, primidone or propranolol therapy. The dosage of zonisamide to these patients was 100 mg to a maximum of 200 mg once daily. The study dose was continued for at least 12 weeks unless discontinued earlier due to side effects. Of the ten patients, who did not respond to other treatment, four patients responded by reduction in tremor of greater than 50% and reported a better quality of life. Amongst other categories: mixed tremor (non-essential, secondary to trauma or multiple sclerosis), two out of two patients responded; multi-infarct-related (2 or more minor strokes) tremor, one out of two patients responded; and in Parkinsonian tremor, two out of four responded.

Example 5 demonstrates that the claimed methods are enabled because zonisamide was used to successfully treat patients with **tremors** induced by several different causes. Moreover, one skilled in the art could practice the claimed invention without undue experimentation based on Example 5 and other information in the specification (e.g., modes of administration, dosing amounts).

Applicant notes that the results in Example 5 in the specification are supported by later-conducted human clinical trials. In the left hand column of the Introduction, Morita et al, *Parkinsonism and Related Disorders*, 11:101-103 (2005)[3] report:

> Our clinical trials confirmed that ZNS [Zonisamide] is effective for symptoms of PD [Parkinson's Disease], particularly tremor. ZNS is effective for tremor in PD patients.... Therefore, ZNS may also be used in treating essential tremor, a representative tremor disorder."

See also Zesiewicz et al, *Movement Disorders*, 22(2):279-282 (2007) at "Discussion" on page 281.[4]

Epilepsy and the claimed tremors are different diseases with different etiologies and different pathologies. Tremors are discussed extensively throughout the specification. The PTO has not established any relationship between the different diseases of epilepsy and tremors that would make Tiara relevant to the pending claims. Moreover, Example 5 in the specification demonstrates that zonisamide was successfully used to treat patients with tremors.

In the Office Action at page 3, lines 3-5, the PTO asserts that there is "no guidance in the instant specification to employ other dosage [sic] different from that employed in the instant specification, Example 5."

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[3] Morita is cited in the Information Disclosure Statement filed concurrently herewith.
[4] Zesiewicz is cited in the Information Disclosure Statement filed concurrently herewith.

Applicant respectfully submits that the PTO's position is contradicted by the specification. At page 7, lines 11-16, the specification teaches:

> The amount of active compound administered depends on the subject being treated, the severity of the affliction, the manner of administration and the judgment of the prescribing physician. However, an effective dosage is in general in the range of 0.5-10 mg/kg/day, preferably 2-10 mg/kg/day which can be administered all at a time or in divided doses. The dosage of these compounds can vary in accordance with the administration route, the age of the patient and the degree of the therapeutic effect desired.

The specification provides guidance to use other dosages that are different from that used in Example 5. Based on the guidance provided in the specification and the working example, the breadth of the claims, and the level of skill in the art, one would be able to find through routine experimentation an appropriate and therapeutically effective dose of zonisamide to administer to patients to treat tremors. The claimed dose need not be limited to the dose used in Example 5 and need not be limited to the dose described in the specification at page 7, lines 11-16. The dose must be "therapeutically effective" and that dose can be determined by routine experimentation based on the extensive guidance and teachings provided in the specification. *See In re Wands*, 858 F.2d 731 (Fed. Cir. 1988).

The standard for determining whether the specification meets the enablement requirement was made in the Supreme Court decision of *Mineral Separation v. Hyde,* 242 U.S. 261 (1916) which posed the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988); *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247 (Fed. Cir. 2004); MPEP 2164.01. Applicant respectfully submits that the PTO is not applying the proper test for enablement in the present application. One skilled in the art could practice the presently claimed methods without undue experimentation in view of the guidance provided in the specification at page 7, lines 11-

16 and Example 5, the breadth of the claims, the level of skill in the art, and the type of experimentation routinely employed by one skilled in the art with respect to patients' medication dosages. Example 5 and page 7, lines 11-16 in the specification provide guidance for one skilled in the art to vary the dosage to determine other therapeutically effective amounts of zonisamide that would be useful for treating tremors. This is nothing more than routine experimentation.

The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993); MPEP 2164.08. All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. *Chiron Corp. v. Genentech, Inc.* at page 1253. The scope of enablement must only bear a reasonable correlation to the scope of the claims. *In re Fisher*, 427 F.2d 833 (CCPA 1970); MPEP 2164.08.

Claims should not be rejected as being broader than the enabling disclosure under 35 U.S.C. § 112 for not including limitations dealing with factors which would be considered obvious to one of ordinary skill in the art to whom the specification and claims are directed. *In re Skrivan*, 427 F.2d 801 (CCPA 1970) ; MPEP 2164.08. One does not look to the claims but to the specification to find out how to practice the claimed invention. *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983); *In re Hyatt*, 708 F.2d 712 (Fed. Cir. 1983); MPEP 2164.08. Limitations and examples in the specification do not generally limit what is covered by the claims. *Chiron Corp. v. Genentech, Inc.* at page 1253; *In re Goffe*, 542 F.2d 564 (CCPA 1976); MPEP 2164.08.

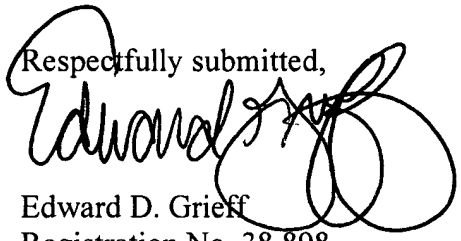
The PTO is asserting that the Applicant must limit the claims to the specific dose of zonisamide described in Example 5 in order to satisfy the enablement requirement. The PTO's

position is untenable in view of established case law. Example 5 in the specification demonstrates that zonisamide is useful for treating tremors, i.e., the claims are enabled. Again, one skilled in the art could, without undue experimentation, rely on Example 5 and other teachings in the specification as guidance to find other dosages of zonisamide that would also be therapeutically effective for treating tremors. Applicant need not limit the claims to that which is described in Example 5 in order to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph.

In view thereof, Applicant respectfully requests that the rejection of claims 12-35 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Applicant respectfully submits that claims 12-35 are in condition for allowance.

Respectfully submitted,



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Date: February 12, 2007

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